

Claims

*Su B2*

1. An intraoral quickly disintegrating tablet comprising a cyclic GMP phosphodiesterase inhibitor and a saccharide.

2. The tablet as claimed in claim 1, which further comprises a binder.

3. A method for manufacturing the tablet defined in claim 1, which comprises mixing a cyclic GMP phosphodiesterase inhibitor with a saccharide, kneading the mixture with an organic solvent, water or an aqueous organic solvent and subjecting it to a compression-molding.

4. The method as claimed in claim 3, which comprises filling the kneaded mixture in a mold and subjecting it to a compression-molding with a film.

5. An intraoral quickly disintegrating tablet comprising a difficultly soluble pharmaceutical agent and a saccharide and further comprising at least one selected from surfactant and a water-soluble polymer.

6. A method for manufacturing the tablet as claimed in claim 5, which comprises dissolving a difficultly soluble pharmaceutical agent in an organic solvent or an aqueous organic solvent together with at least one selected from a surfactant and a water-soluble polymer, coating the solution on a filler or granulating it with a filler to obtain molded products, mixing a saccharide with them, adding an organic solvent, water

or an aqueous organic solvent thereto, followed by kneading, and subjecting it to a compression-molding.

7. A method for manufacturing the tablet as claimed in claim 5, which comprises adding at least one selected from a surfactant and a water-soluble polymer and a saccharide to a difficultly soluble pharmaceutical agent, followed by mixing, adding an organic solvent, water or an aqueous organic solvent thereto, followed by kneading, and subjecting it to a compression-molding.

8. The method for manufacturing as claimed in claim 6, wherein the molded products are granules, fine granules or powder.

9. The method for manufacturing as claimed in claim 6, in which the granulation-molding is carried out, using a fluidized bed granulator, a tumbling granulator, an extrusion granulator or a spray-drying granulator.

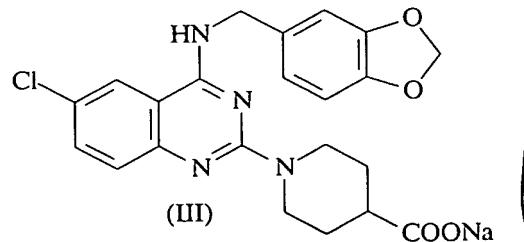
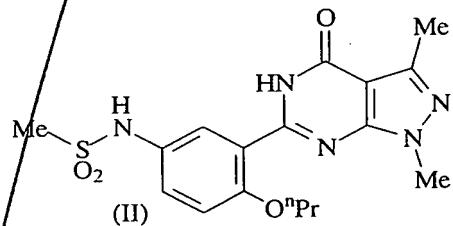
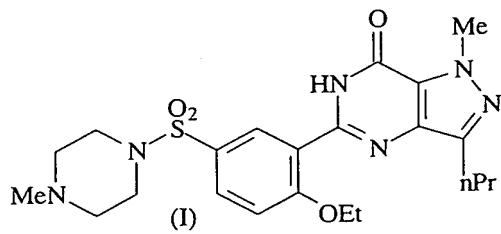
10. The method for manufacturing as claimed in claim 6 or 7, which comprises filling the powder kneaded with the organic solvent, water or the aqueous organic solvent in a mold and subjecting it to compression-molding with a film in the compression-molding stage.

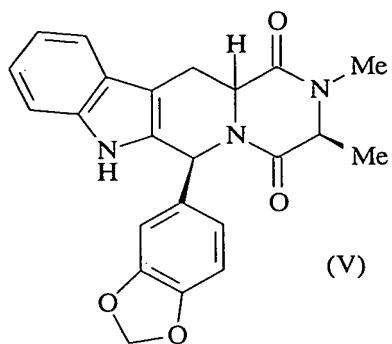
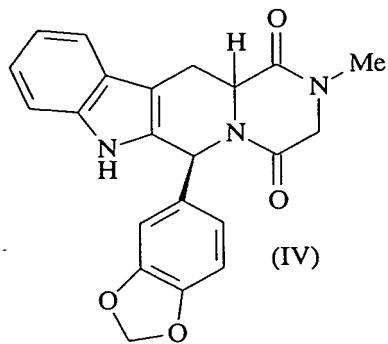
11. The tablet as claimed in claim 5, wherein the slightly soluble pharmaceutical agent is a cyclic GMP phosphodiesterase inhibitor.

12. The method for manufacturing as claimed in claim 6 or 7, wherein the slightly soluble pharmaceutical agent is a

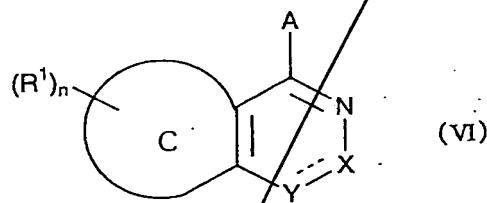
*A2*  
*cut* cyclic GMP phosphodiesterase inhibitor.

*Cut*  
*B3* 13. The tablets as claimed in any of claims 1, 2 and 11, wherein the cyclic GMP phosphodiesterase inhibitor is 5-[2-ethoxy-5-(4-methyl-1-piperazinylsulfonyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one represented by the formula (I), 1,3-dimethyl-5-(2-propoxy-5-methanesulfonamidophenyl)-1,5-dihdropyrazolo[3,4-d]pyrimidin-4-one represented by the formula (II), 2-(4-carboxypiperidino)-4-(3,4-methylenedioxybenzyl)amino-6-chloroquinazoline represented by the formula (III), (6R,12aR)-2,3,6,7,12,12a-hexahydro-2-methyl-6-(3,4-methylenedioxyphenyl)-pyrazino[2',1':6,1]pyrido[3,4-b]indol-1,4-dione represented by the formula (IV), (3S,6R,12aR)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-6-(3,4-methylenedioxyphenyl)-pyrazino[2',1':6,1]pyrido[3,4-b]indol-1,4-dione shown by the formula (V) or a pharmacologically acceptable salt thereof.



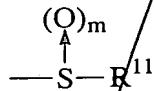


14. The tablet as claimed in any of claims 1, 2 and 11, wherein the cyclic GMP phosphodiesterase inhibitor is a compound represented by the following formula (VI) or a pharmacologically acceptable salt thereof, i.e. a fused pyridazine compound represented by the following formula or a pharmacologically acceptable salt thereof.



in the formula, the ring C is an unsaturated 5- or 6-membered ring which may have a hetero atom; n is 0 or an integer of 1-4; R<sup>1</sup> is a halogen atom, an optionally substituted lower alkyl group, an optionally substituted lower alkoxy group, an optionally substituted cycloalkyl group, nitro group, cyano group, a group represented by the formula -NR<sup>2</sup>R<sup>3</sup> (in the formula, R<sup>2</sup> and R<sup>3</sup> are the same as or different from each other and each is hydrogen atom, an optionally substituted lower alkyl group, an acyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group. R<sup>2</sup> and R<sup>3</sup> may form a ring

together with a nitrogen atom bonded thereto. The ring may further have a substituent), a group represented by the formula -O-R<sup>9</sup> (in the formula, R<sup>9</sup> is hydrogen atom, an optionally substituted lower alkyl group, an acyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group), a group represented by the formula -S-R<sup>10</sup> (in the formula, R<sup>10</sup> is hydrogen atom, an optionally substituted lower alkyl group, an acyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group), a group represented by the formula (VII):



(in the formula (VII), R<sup>11</sup> is hydrogen atom, a lower alkyl group or amino group; and m is 0 or an integer of 1-2) or an optionally protected carboxyl group, and when n is 2-4, R<sup>1</sup> may independently have the above-mentioned substituent; A is hydrogen atom, a halogen atom, a group represented by the formula -NR<sup>4</sup>R<sup>5</sup> (in the formula, R<sup>4</sup> and R<sup>5</sup> are the same as or different from each other and each is hydrogen atom, an optionally substituted lower alkyl group, an acyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group, or R<sup>4</sup> and R<sup>5</sup> may form a ring together with a nitrogen atom bonded thereto. The ring may further have a substituent), an optionally substituted aryl group, an optionally substituted heteroaryl group, an optionally substituted arylalkyl group or an

optionally substituted heteroarylalkyl group; X is a group represented by the formula  $-NR^6-$  (in the formula,  $R^6$  is hydrogen atom, an optionally substituted lower alkyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group) or a group represented by the formula  $-N=$ ; Y is a group represented by  $-CO-$  or a group represented by the formula  $-C(B)=$  (in the formula, B is hydrogen atom, a halogen atom, a formula represented by the formula  $-NR^7R^8$  (in the formula,  $R^7$  and  $R^8$  may be the same as or different from each other and each is hydrogen atom, an optionally substituted lower alkyl group, an acyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group.  $R^7$  and  $R^8$  may form a ring together with a nitrogen atom bonded thereto. The ring may further have a substituent), a group represented by the formula  $-O-R^{12}$  (in the formula,  $R^{12}$  is hydrogen atom, an optionally substituted lower alkyl group, an acyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group), a group represented by the formula  $-S-R^{13}$  (in the formula,  $R^{13}$  is hydrogen atom, an optionally substituted lower alkyl group, an acyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group), an optionally substituted aryl group, an optionally substituted heteroaryl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group); and the formula (VIII) ----- means a double or single bond, provided that when the ring C

is a benzene ring, the case where n is 0 is excluded.

15. The tablet as claimed in claim 14, wherein the compound represented by the formula (VI) is

4 - (3 - chloro - 4 - methoxybenzyl) amino - 6 - cyano - 1 - (4 - hydroxypiperidino) phthalazine hydrochloride represented by the formula (IX),

4 - (3 - chloro - 4 - methoxyphenethyl) amino - 6 - cyano - 1 - (4 - hydroxypiperidino) phthalazine hydrochloride represented by the formula (X),

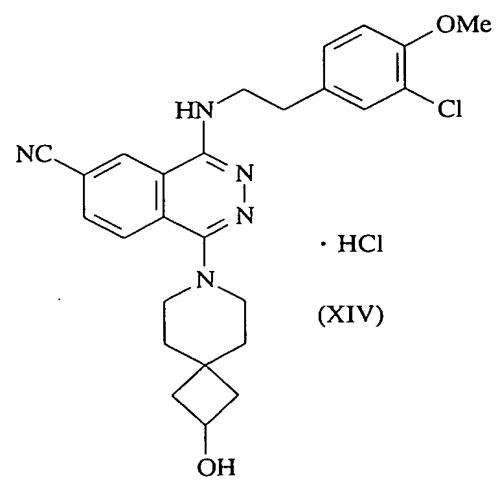
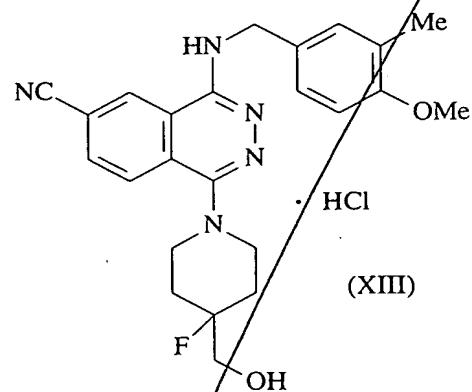
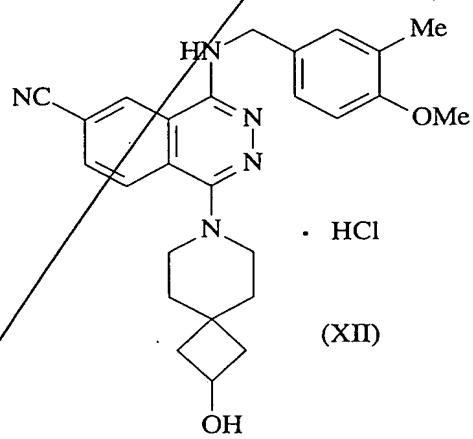
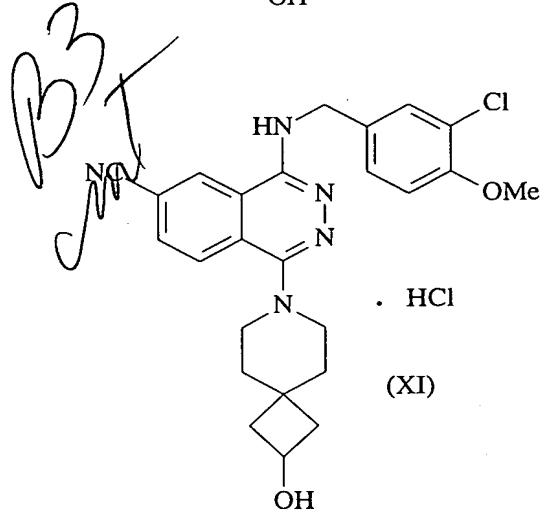
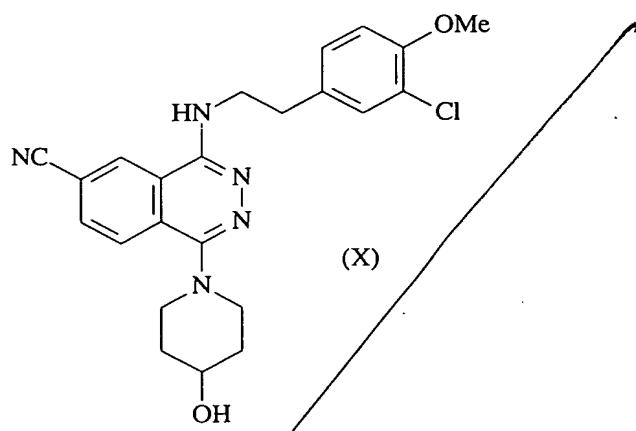
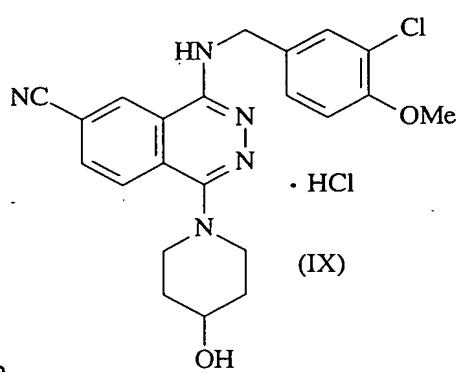
4 - [(3 - chloro - 4 - methoxybenzyl) amino] - 1 - (2 - hydroxy - 7 - azaspiro[3,5]non-7-yl) - 6 - phthalazine carbonitrile hydrochloride represented by the formula (XI),

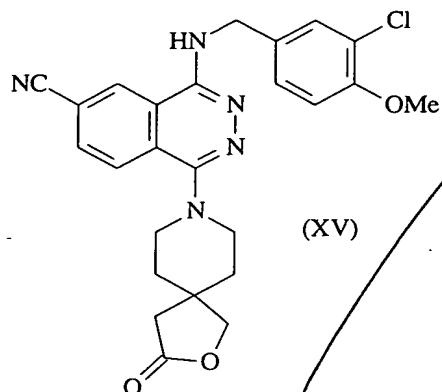
1 - (2 - hydroxy - 7 - azaspiro[3,5]non-7-yl) - 4 - [(4 - methoxy - 3 - methylbenzyl) amino] - 6 - phthalazine carbonitrile hydrochloride represented by the formula (XII),

1 - [4 - fluoro - 4 - (hydroxymethyl) piperidino] - 4 - [(4 - methoxy - 3 - methylbenzyl) amino] - 6 - phthalazine carbonitrile hydrochloride represented by the formula (XIII),

4 - [(3 - chloro - 4 - methoxyphenethyl) amino] - 1 - (2 - hydroxy - 7 - azaspiro[3,5]non-7-yl) - 6 - phthalazine carbonitrile hydrochloride shown by the formula (XIV) or

4 - [(3 - chloro - 4 - methoxybenzyl) amino] - 1 - (3 - oxo - 2 - oxa - 8 - azaspiro[4,5]decen-8-yl) - 6 - phthalazine carbonitrile represented by the formula (XV).





16. The tablet as claimed in any of claims 1, 2 and 5, wherein the saccharide is at least one selected from mannitol, sucrose, lactose, trehalose, xylitol, erythritol, glucose, starch and dextrin.

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17. The method for manufacturing as claimed in any of claims 3, 4 and 12, wherein the cyclic GMP phosphodiesterase inhibitor is 5-[2-ethoxy-5-(4-methyl-1-piperazinylsulfonyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one represented by the formula (I), a compound represented by the formula (VI) or pharmacologically acceptable salts thereof.